Claims 1-14 and 16-24 were pending before this response. By the present communication, claim 16 is canceled without prejudice and claims 1 and 17 are amended to define Applicants' invention with greater particularity. These amendments add no new matter as the new claim language is fully supported by the specification and original claims. Accordingly, claims 1-14 and 17-24 are pending as shown in attached Exhibit A.

The Objection to the Specification

The Office Action states that the Specification is objected to because it refers to the biological deposits at ATCC without indicating an ATCC Deposit No. By the present communication, the Specification is amended at page 2 bottom paragraph and at page 6, lines 4-21, to delete the paragraphs that refer to a biological deposit with the ATCC. Therefore, Applicants respectfully submit that the grounds for the objection to the Specification have been overcome and withdrawal of the objection is respectfully requested.

The Rejection under 35 U.S.C. § 112, First Paragraph

A. Applicants respectfully traverse the rejection of claim 1 under 35 U.S.C. § 112, First Paragraph, for containing subject matter allegedly not described in the Specification in such a way as to reasonably convey that the inventors had possession of the invention at filing of the Application. In particular, the Examiner asserts that claim 1 "recites DNA sequences comprising at least 25 nucleotides encoding an aminotransferase of SEQ ID NOS: 25-32." Applicants respectfully submit that this interpretation of the final clause of claim 1 is misleading. In fact, clause (d) of claim 1 recites "fragments of a), b) or c) that are at least 15 bases in length and that hybridize to DNA which encodes the amino acid sequences of SEQ ID NOS:25-32 under moderate to highly stringent conditions." Thus, the nucleic acid fragments of clause (d) of claim 1 would be complementary to (i.e. hybridize to) the polynucleotides that encode the enzymes having amino acid sequences as set forth in SEQ ID NOS 25-32.

Thus, the polynucleotide fragments of clause (d) of claim 1 are substantially overlapping in subject mater with those of claim 17. Accordingly, Applicant has amended claim 1 to delete clause (d), thus removing the grounds for the Examiner's rejection of claim 1 under 35 U.S.C. §112, First Paragraph. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

B. Applicants respectfully traverse the rejection of claims 1-14 and 17-24 under 35 U.S.C. §112, First Paragraph, for allegedly lacking an enabling description in the Specification. Applicants disagree with the Examiner's assertion that

> "it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable.

(Office Action, page 5). Applicants respectfully submit that those of skill in the art at the filing of the present application would not have expected to utilize the present invention, as defined by amended claims 1-14 and 17-24, in the manner suggested by the Examiner (i.e., by site-directed mutagenesis of a single polynucleotide that encodes a known enzyme to obtain a different protein that might have aminotransferase enzymatic activity). Since the advent of high throughput screening and library mutagenesis techniques, the single molecule approach has been viewed as archaic. In fact, at the filing of the present application, it was routine for those of skill in the art to screen a library of polynucleotides. For example probes developed from a known polynucleotide sequence (i.e. complementary to a target area of a known polynucleotide sequence) could be used to locate new polynucleotides having similarity of structure (i.e., 70% sequence identity) to the known sequence from biological samples. In addition, given Applicants' nucleotide sequences of SEQ ID NOS:25-32, those of skill in the art could readily have searched publicly available data bases using such sequence alignment programs such as the BLASTN program of the National Center for Biotechnology Information to find sequences with at least 70% identity to Applicants' sequences. The enzymatic function of the proteins expressed using the polynucleotides so identified could have similarly been routinely tested by those of

skill in the art by screening a library of putative enzymes using a known test for aminotransferase activity, such as is disclosed by Applicants in the Specification.

Thus, Applicants respectfully submit that the predictability in such an approach is assessed, not in terms of a single molecule, but in terms of the likelihood that a hybridization match will be found when a very large number of polynucleotides is screened using techniques disclosed by Applicants and as known in the art, and further in view of the likelihood that a molecule having the desired activity will be found when a very large number of molecules is submitted to the known test. Applicants respectfully submit that neither undue knowledge nor undue effort is required to perform such mutagenesis and screening techniques.

Applicants respectfully submit, therefore, that those of average skill in the art could use the techniques disclosed in the Specification and known in the art at the filing of the present application to make and use the invention, as defined by amended claims 1-14 and 17-24 without undue experimentation. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

The Rejection Under 35 U.S.C. § 112, Second Paragraph

Applicants respectfully traverse the rejection of claims 1, 16, and 17-24 under 35 U.S.C. §112, Second Paragraph, as allegedly being indefinite. With regard to the alleged indefiniteness of claim 1(d), claim 1 has been amended by the present communication to delete clause (d) from claim 1, thus obviating the rejection as to this point. With regard to the alleged indefiniteness of claim 16, by the present communication claim 16 is canceled without prejudice.

With regard to the alleged indefiniteness of the term "probe," as used in claims 17-24, Applicants traverse the Examiner's assertion that Applicants' use of the term "probe" is unclear because it cannot be determined whether use of the term "imparts any limitations (either structural or functional) on the nucleic acids claimed," such as a requirement that the nucleic acid "probe" is "labeled" (Office Action, pages 5-6). Claim 17 does not require that the probe be detectable, only that the target:probe duplex is "detectable." Those of skill in the art would

understand that detectable labeling of the probe to achieve a detectable target:probe duplex is optional. It was well known in the art at the filing of the present application, for example, that the product of a hybridization reaction has a different molecular weight than that of the probe and formation of the duplex is readily detectable using any of a variety of chromatography or separation techniques based on the difference in molecular weight between the unbound probe and the target:probe duplex. Thus, Applicants respectfully submit that it would be clear to those of skill in the art that the term "probe" as used in claims 17-24 does not *require* that the probe comprise a label in order for the hybridization product of the target:probe duplex to be "detectable," although in certain embodiments the nucleic acid probe may additionally comprise a detectable label, as required in claim 24.

In addition, Applicants traverse the Examiner's assertion that the phrase "moderate to highly stringent" is indefinite because it allegedly is unclear how homologous to the sequence of a gene encoding SEQ ID NOS:25-32 a sequence must be to be included within the scope of claims 17-24. Applicants respectfully submit that the terms "moderate to highly stringent" as applied to hybridization conditions would be judged by those of skill in the art with reference to Applications example in description on pages 8-9 of the Specification of a set of "stringent" conditions. However, to expedite prosecution and reduce the issues by the present communication, claims 17-24 have been amended to require hybridization "under conditions that include 0.9 M NaCl, 5.0 mM NaH_2PO_4, 5.0 mM Na_2 EDTA, 0.5% SDS and 10 X Denhardt's at about 45° C."

In view of these amendments, Applicants respectfully submit that claims 1-14 and 17-24 meet all requirements under 35 U.S.C. § 112, Second Paragraph.

The Double Patenting Rejection

Applicants traverse the rejection of claims 1-14 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U. S. Patent No. 5,814,473. Submitted herewith is a Terminal Disclaimer disclaiming the terminal part of any patent granted on the above-identified Application No. 09/481,733 that would extend beyond the

expiration date of U.S. Patent No. 5,814,473. Such Terminal Disclaimer shall be enforceable only for and during such period that the legal title to claims 1-14 of U. S. Patent No. 5,814,473 is the same as the legal title to the above application. In view of the Terminal Disclaimer submitted herewith, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-14 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-14 of U.S. Patent No. 5,814,473.

In addition, Applicants traverse the rejection of claims 1-14 and 17-24 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U. S. Patent No. 6,013,509. Submitted herewith is a Terminal Disclaimer disclaiming the terminal part of any patent granted on the above-identified Application No. 09/481,733 that would extend beyond the expiration date of claims 1-10 of U.S. Patent No. 6,013,509. Such Terminal Disclaimer shall be enforceable only for and during such period that the legal title to claims 1-10 of U. S. Patent No. 6,013,509 is the same as the legal title to the above application.

In view of the Terminal Disclaimer submitted herewith, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-14 and 17-24 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-14 of U.S. Patent No. 5,814,473 and claims 1-10 of U.S. Patent No. 6,013,509.

Information Disclosure Statement

Applicants request that the initialed PTO 1449 mailed with the Information Disclosure Statement to the United States Patent Office on August 23, 2000 indicating that the Examiner has reviewed the references submitted therewith be returned.

In view of the above amendments and remarks, reconsideration and favorable action on claims 1-14 and 17-24 are respectfully requested. In the event any matters remain to be resolved in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

In view of the above remarks, reconsideration and favorable action on all claims is respectfully requested. Should any questions remain in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

Date: 4/27/01

Lisa A. Haile, Ph.D.
Registration No. 38,347
Telephone: (858) 677-1456
Facsimile: (858) 677-1465

GRAY, CARY, WARE & FREIDENRICH LLP
4365 Executive Drive, Suite 1600
San Diego, California 92121-2189
USPTO Customer No. 28213

Attachment – Exhibit A

EXHIBIT A

The pending claims as amended in this Response

1. (Amended) An isolated polynucleotide encoding an enzyme with aminotransferase activity and which is at least 70% identical to a member selected from the group consisting of:

a) SEQ ID NOS:25-32;

b) SEQ ID NOS:25-32 wherein T can also be U; and

c) nucleic acid sequences complementary to a) and b)[; and

d) fragments of a), b) or c) that are at least 15 bases in length and that hybridize to DNA which encodes the amino acid sequences of SEQ ID NOS:25-32 under moderate to highly stringent conditions].

17. (Amended) A nucleic acid probe comprising an oligonucleotide from about 10 to 50 nucleotides in length and having an area of nucleotides that is at least 70% complementary to a nucleic acid target region of a nucleic acid encoding an amino acid sequence selected from the group consisting of SEQ ID NOS:25-32 and which hybridizes to the nucleic acid target region [under moderate to highly stringent conditions] to form a detectable target:probe duplex under conditions that include 0.9 M NaCl, 5.0 mM NaH_2PO_4, 5.0 mM Na_2 EDTA, 0.5% SDS and 10 X Denhardt's at about 45° C.